DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

Our Reference Number: 96-0597

March 25, 1999

Peter Bonne Eriksen, Ph.D.
Novo Nordisk A/S
Novo Alle
DK-2880 Bagsvaerd
DENMARK

Dear Dr. Eriksen:

Enclosed please find U.S. License No.1261 issued in accordance with the provisions of Section 351(a) of the Public Health Service Act, as amended November 21, 1997 (FDAMA; Public Law 105-115). This license authorizes Novo Nordisk A/S to manufacture and introduce into interstate commerce Coagulation Factor VIIa (Recombinant) [NovoSeven®] for which your company has demonstrated compliance with establishment and product standards. Coagulation Factor VIIa (Recombinant) is indicated for use in the treatment of bleeding episodes in hemophilia A or B patients with inhibitors to Factor VIII or Factor IX.

Under this license you are authorized to introduce into interstate commerce Coagulation Factor VIIa (Recombinant) in dosage strengths of 1.2, 2.4 and 4.8 mg per vial. Changes to the product, production process, location of production process, equipment, facilities, or responsible personnel are required to be reported to FDA as specified in Title 21 Code of Federal Regulations (CFR) Section 601.12.

We acknowledge your commitment to implement a post marketing surveillance program and your March 17, 1999 letter describing the agreements with regard to this registry. Reports containing the information obtained by the registry will be submitted annually.

The dating period for this product shall be 24 months from the date of manufacture when stored at 2-8° C. The date of manufacture shall be defined as the date of the initial sterile filtration of the formulated bulk. We acknowledge your March 15, 1999 commitment to submit the results of ongoing stability studies at six month intervals.

All adverse experience reports should be submitted according to 21 CFR 600.80 to the Center for Biologics Evaluation and Research (CBER), HFM-210, Food and Drug Administration, 1401 Rockville Pike, Rockville, Maryland 20852-1448. In addition, safety related information

obtained in the course of the ongoing clinical studies should be reported to [redacted] in accordance with 21 CFR 312.32. It is also requested that distribution reports be submitted according to 21 CFR 600.81.

Coagulation Factor VIIa (Recombinant) manufactured by Novo Nordisk A/S is exempt from the lot release requirements of 21 CFR 610.2. Novo Nordisk A/S shall submit three (3) vials of each of the first ten lots of Coagulation Factor VIIa (Recombinant) released for distribution in the U.S.

Please submit three (3) copies of final printed labeling at the time of use accompanied by Part II of FDA 2567 with completed implementation information. In addition, you may wish to submit your proposed introductory advertising and promotional campaign. If so, please submit three (3) copies of the proposed material in draft form with Part I of the FDA Form 2567/2253 to CBER, Advertising and Promotional Labeling Staff (APLS), HFM-602, 1401 Rockville Pike, Rockville, Maryland 20852-1448. Promotional claims should be consistent with and not contrary to the approved labeling. No comparative claims or claims of superiority over other similar products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research. Final copies of advertising and promotional materials should be submitted at the time of use with Part II of FDA Form 2567/2253 to APLS. Please include copies of the approved labeling with your proposed or final copy of advertising and promotional materials submitted to CBER.

Please acknowledge receipt of the enclosed License to the Director, Division of Blood Applications, HFM -370, Center for Biologics Evaluation and Research, 1401 Rockville Pike, Rockville, Maryland 20852-1448.

Sincerely yours,

Jay S. Epstein, M.D.
Director
Office of Blood Research and Review
Center for Biologics Evaluation
and Research

Steven A. Masiello
Acting Director
Office of Compliance
and Biologics Quality
Center for Biologics Evaluation
and Research